

***Haemophilus influenzae* type B**

Haemophilus influenzae was first described by Pfeiffer in 1892. During a major outbreak of influenza, he found the bacteria in the sputum of patients, and proposed a causal association between this species and the clinical syndrome known as influenza. The organism was given the name *Haemophilus* by Winslow, et al., in 1920. It was not until 1933 that Smith, et al., established that influenza was caused by a virus and that *H. influenzae* was a cause of secondary infection.

In the 1930s, Margaret Pittman showed that *H. influenzae* could be isolated in encapsulated and unencapsulated forms. She identified six capsular types (a-f), and observed that virtually all isolates from cerebrospinal fluid (CSF) and blood were of the capsular type b.

Before the introduction of effective vaccines, *H. influenzae* type b (Hib) was the leading cause of bacterial meningitis and other invasive bacterial disease among children <5 years of age. Almost all serious Hib infections were among children <5 years of age; approximately one in 200 children developed invasive Hib disease before the age of 5 years. Two-thirds of cases were among children <18 months of age.

Haemophilus influenzae

Haemophilus influenzae is a gram-negative coccobacillus. It is generally aerobic, but can grow as a facultative anaerobe. In vitro growth requires accessory growth factors, including “X” factor (hemin) and “V” factor (nicotinamide adenine dinucleotide [NAD]).

Chocolate agar media are used for isolation. *H. influenzae* will generally not grow on blood agar, which lacks NAD.

The outermost structure of *H. influenzae* is composed of polyribosyl-ribitol phosphate (PRP), a polysaccharide, which is responsible for virulence and immunity. Six antigenically and biochemically distinct capsular polysaccharide serotypes have been described, which are designated types a through f. In the prevaccine era, type b organisms accounted for 95% of all strains that cause invasive disease.

PATHOGENESIS

The organism enters the body through the nasopharynx. Organisms colonize the nasopharynx and may remain only transiently or for several months in the absence of symptoms (“asymptomatic carrier”). In the prevaccine era, Hib could be isolated from the nasopharynx of 0.5%-3% of normal infants and children, uncommonly in adults. Nontypable (unencapsulated) strains are also frequent inhabitants of the human respiratory tract and are generally non-invasive.

In some persons the organism causes an invasive infection. The exact mode of invasion to the

blood stream is unknown. Antecedent viral or mycoplasma infection of the upper respiratory tract may be a contributing factor. The bacteria spread in the bloodstream to distant sites in the body. Meninges are especially likely to be affected.

The most striking feature of Hib disease is **age-dependent susceptibility**. Passive protection of some infants is provided by transplacentally acquired maternal IgG antibodies and breast-feeding during the first 6 months of life. Peak attack rates occur at 6-7 months of age, declining thereafter. Hib disease is uncommon beyond 5 years of age. The presumed reason for this age distribution is the acquisition of humoral immunity to Hib with increasing age.

Antibodies to Hib capsular polysaccharide are protective. The precise level of antibody required for protection against invasive disease is not clearly established. However, a titer of 1 µg/mL 3 weeks postvaccination correlated with protection in studies following vaccination with unconjugated PRP vaccine and suggested long-term protection from invasive disease.

Acquisition of both anticapsular and serum bactericidal antibody is inversely related to the age-specific incidence of Hib disease.

In the pre-vaccine era, most children acquired “natural” immunity by 5-6 years of age through asymptomatic infection by Hib bacteria. Since only a relatively small proportion of children carry Hib at any time, it has been postulated that exposure to organisms that share common antigenic structures with the capsule of Hib (so-called “cross-reacting organisms”) may also stimulate the development of anticapsular antibodies against Hib. Natural exposure to Hib also induces antibodies to outer membrane proteins, lipopolysaccharides, and other antigens on the surface of the bacterium.

The genetic constitution of the host may also be important in susceptibility to infection with Hib. Risk for Hib disease has been associated with a number of genetic markers, but the mechanism of these associations is unknown. No single genetic relationship regulating susceptibility or immune responses to polysaccharide antigens has yet been convincingly demonstrated.

CLINICAL FEATURES

Invasive disease caused by *H. influenzae* type b can affect many organ systems. The most common types of invasive disease are meningitis, epiglottitis, pneumonia, arthritis, and cellulitis.

Meningitis is infection of the membranes covering the brain and is the most common clinical manifestation of invasive Hib disease, accounting for 50%-65% of cases in the prevaccine era. Hallmarks of Hib meningitis are fever, decreased mental status, and stiff neck. The mortality rate is 2%-5%, despite appropriate antimicrobial therapy. Neurologic sequelae occur in 15%-30% of survivors.

Epiglottitis is an infection and swelling of the epiglottis, the tissue in the throat that covers and protects the larynx during swallowing. Epiglottitis may cause life-threatening airway

obstruction.

Septic arthritis (joint infection), **cellulitis** (rapidly progressing skin infection which usually involves face, head, or neck), and **pneumonia** (which can be mild focal or severe empyema) are common manifestations of invasive disease.

Osteomyelitis (bone infection), and **pericarditis** (infection of the sac covering the heart) are less common forms of invasive disease. Otitis media and acute bronchitis due to *H. influenzae* are generally caused by nontypable strains. Hib strains account for only 5%-10% of *H. influenzae* causing otitis media.

LABORATORY DIAGNOSIS

A **gram stain** of an infected body fluid may demonstrate small gram-negative coccobacilli suggestive of invasive *Haemophilus* disease. Cerebrospinal fluid (CSF), blood, pleural fluid, joint fluid, and middle ear aspirates should be cultured on the appropriate media. A positive culture for *Haemophilus influenzae* establishes the diagnosis.

All isolates of *Haemophilus influenzae* should be serotyped. This is an extremely important laboratory procedure that should be performed on every isolate of *Haemophilus influenzae*, especially those obtained from children <15 years of age. This test determines whether an isolate is type b, and is important because only type b is potentially vaccine preventable. Serotyping is usually done by either the state health department laboratory or a reference laboratory.

Antigen detection may be used as an adjunct to culture, particularly in the diagnosis of patients who have been partially treated with antimicrobials and the organism may not be viable on culture. Two types are available.

Latex agglutination is a rapid, sensitive, and specific method to detect Hib capsular polysaccharide antigen in CSF, serum, urine, pleural fluid, joint fluid, etc.

Counterimmunoelectrophoresis (CIE) is similar to latex agglutination, but is less sensitive, takes longer, and is more difficult to perform.

MEDICAL MANAGEMENT

Hospitalization is generally required. Antimicrobial therapy with chloramphenicol or an effective third-generation cephalosporin (cefotaxime or ceftriaxone) should be begun immediately. Treatment course is usually 10 to 14 days.

Ampicillin-resistant strains of Hib are now common throughout the United States. Children with life-threatening illness in which Hib may be the etiologic agent should not receive ampicillin as initial empiric therapy.

EPIDEMIOLOGY

Occurrence

Hib disease occurs worldwide. However, the incidence outside the United States and Europe has not been determined.

Reservoir

Humans (asymptomatic carriers) are the only known reservoir. Hib does not survive in the environment on inanimate surfaces.

Transmission

Primary mode is presumably by respiratory droplet spread, although firm evidence for this mechanism is lacking.

Temporal pattern

Several studies in the prevaccine era described a bimodal seasonal pattern in the United States, with one peak between September and December, and a second peak between March and May. The reason for this bimodal pattern is not known.

Communicability

The contagious potential of invasive Hib disease is considered to be limited. However, certain circumstances, particularly close contact with a case (e.g., household, day-care, or institutional setting) can lead to outbreaks or direct secondary transmission of the disease.

SECULAR TRENDS IN THE UNITED STATES

Haemophilus influenzae infections became nationally reportable in 1991. Serotype-specific reporting continues to be incomplete.

Prior to the availability of national reporting data, several areas carried out active surveillance for H. influenzae disease, which allowed estimates of disease nationwide. In the early 1980s, it was estimated that about 20,000 cases occurred annually in the United States, primarily among children younger than 5 years of age (40-50 cases per 100,000 population). The incidence of invasive Hib disease began to fall dramatically in the late 1980s, coincident with licensure of conjugate Hib vaccines, and has declined by >99% compared to the prevaccine era.

From 1996 through 2000, an average of 1,247 invasive *Haemophilus influenzae* cases were reported to CDC in all age groups (range 1,162-1,398 per year). Of these, an average of 272 (approximately 22%) per year were among children <5 years of age. Serotype was known for

76% of the invasive cases among children age <5 years. Three-hundred-forty-one (average of 68 cases per year) were due to type b.

There is evidence that Hib vaccines decrease the rate of carriage of Hib among vaccinated children, therefore decreasing the chance that unvaccinated children will be exposed.

Incidence is strikingly age-dependent. In the prevaccine era, up to 60% of invasive disease occurred before age 12 months, with a peak occurrence in children 6-11 months of age. Children over 60 months of age account for <10% of invasive disease.

In 1998-2000, approximately 44% of children less than 5 years of age with confirmed invasive Hib disease were less than 6 months of age, and too young to have completed a three-dose primary vaccination series. Fifty-six percent were age 6 months or older, and were eligible to have completed the primary vaccination series. Of these age-eligible children, 68% were either incompletely vaccinated (<3 doses) or their vaccination status was unknown. Thirty-two percent of children aged 6-59 months with confirmed type b disease had received 3 or more doses of Hib vaccine, including 22 who had received a booster dose 14 or more days prior to onset of their illness. The cause of Hib vaccine failure in these children is not known.

Risk factors for Hib disease include host factors and exposure factors that increase the likelihood of exposure to Hib. Exposure factors include household crowding, large household size, day-care attendance, low socioeconomic status, low parental education levels, and school-aged siblings. Host factors include race/ethnicity (elevated risk in blacks, Hispanics, Native Americans — possibly confounded by socioeconomic variables that are associated with both race/ethnicity and Hib disease), chronic diseases (e.g., sickle cell anemia, antibody deficiency syndromes, malignancies, especially during chemotherapy), and possibly gender (male > female).

Protective factors (effect limited to <6 months of age) include breast-feeding and passively acquired maternal antibody.

Secondary Hib disease is defined as illness within 1-60 days following contact with an ill child, and accounts for less than 5% of all invasive Hib disease. Among household contacts, six studies have found a secondary attack rate of 0.3% in the month following disease onset of the index case, which is about 600-fold higher than the risk for the general population. Attack rates varied substantially with age, from 3.7% among children under 2 years of age to 0% among contacts over the age of 6 years. In these household contacts, 64% of secondary cases occurred within the first week (excluding the first 24 hours) of disease onset in the index case, 20% during the second week, and 16% during the third and fourth weeks.

There are conflicting data regarding the risk of secondary transmission among **day-care contacts**. Secondary attack rates have varied from 0% to as high as 2.7%. Most studies seem to suggest that day-care contacts are at relatively low risk for secondary transmission of Hib disease.

HAEMOPHILUS INFLUENZAE TYPE B VACCINE

Characteristics

A pure polysaccharide vaccine (HbPV) was licensed in the United States in 1985. The vaccine was not effective among children younger than 18 months of age. Estimates of efficacy in older children varied widely, from 88% to -69% (a negative efficacy implies greater disease risk for vaccinees than nonvaccinees). HbPV was used until 1988, but is no longer available in the United States.

The characteristics of the Hib polysaccharide were similar to other polysaccharide vaccines (e.g., pneumococcal, meningococcal). The response to the vaccine was typical of a T-independent antigen, most notably an age-dependent response, and poor immunogenicity in children <2 years of age. In addition, no boost in antibody titer was observed with repeated doses, the antibody which was produced was relatively low-affinity IgM, and switching to IgG production was poor.

Haemophilus influenzae type b polysaccharide-protein conjugate vaccines

Conjugation is the process of chemically bonding a polysaccharide (a poor antigen) to a protein “carrier,” which is a more effective antigen. This process changes the polysaccharide from a T-independent to a T-dependent antigen, and greatly improves immunogenicity, particularly in young children. In addition, repeat doses of Hib conjugate vaccines elicit booster responses, and allow maturation of class-specific immunity with predominance of IgG antibody. The Hib conjugates also cause carrier priming and elicit antibody to “useful” carrier protein.

The first Hib conjugate vaccine (PRP-D, ProHIBIT) was licensed in December 1987. This vaccine was not consistently immunogenic in children <18 months of age, and is not recommended for use in infants.

Since 1990, four additional conjugate Hib vaccines have been licensed for use in infants as young as 6 weeks of age. Three of these vaccines are chemically and immunologically distinct (ActHIB and OmniHIB are identical vaccines marketed by different companies). Two combination vaccines that contain Hib conjugate vaccine are also available (see below).

Haemophilus influenzae type b Conjugate Vaccines

Vaccine	Protein Carrier	Manufacturer
PRP-D (ProHIBIT®)	Diphtheria toxoid	Connaught Labs
HbOC (HibTITER®)	Mutant diphtheria protein	Laderle/Praxis
PRO-T (ActHIB® or OmniHIB®)	Tetanus toxoid	Aventis Pasteur
PRP-OMP (PedvaxHIB®)	Meningococcal group B outer membrane protein	Merck & Co., Inc.

Immunogenicity and vaccine efficacy

All three Hib conjugate vaccines licensed for use in infants are highly immunogenic. More than 95% of infants will develop protective antibody levels after a primary series of 2 or 3 doses. Clinical efficacy has been estimated at 95% to 100%. Invasive Hib disease in a completely vaccinated infant is very rare.

Hib vaccine is immunogenic in patients with increased risk for invasive disease, such as those with sickle-cell disease, leukemia, human immunodeficiency virus (HIV) infection, and in those who have had splenectomies. However, in persons with HIV infection, immunogenicity varies with stage of infection and degree of immunocompromise. Efficacy studies have not been performed in populations with increased risk of invasive disease.

VACCINATION SCHEDULE AND USE

All infants, including those born prematurely, should receive a primary series of conjugate Hib vaccine (separate or in combination), beginning at 2 months of age. The number of doses in the primary series depends on the type of vaccine used. A primary series of PRP-OMP (PedvaxHIB) vaccine is two doses; HbOC (HibTiTER) and PRP-T (ActHIB) require a three-dose primary series (See table below). A booster is recommended at 12-15 months regardless of which vaccine is used for the primary series.

**ACIP-Recommended *Haemophilus influenzae* type b (Hib)
Routine Vaccination Schedule**

Vaccine	2 Months	4 Months	6 Months	12-15 Months
HbOC	Dose 1	Dose 2	Dose 3	Booster
PRP-T	Dose 1	Dose 2	Dose 3	Booster
PRP-OMP	Dose 1	Dose 2		Booster

The optimal interval between doses is 2 months, with a **minimum interval** of 4 weeks. At least 8 weeks should separate the booster dose from the previous (2nd or 3rd) dose. Hib vaccines may be given simultaneously with all other vaccines.

Recent data suggest that if Hib conjugate vaccines are given before 6 weeks of age, they may induce immunologic tolerance to additional doses of Hib vaccine. A dose given before 6 weeks of age may make the child incapable of responding to subsequent doses. As a result, **Hib vaccines, including combination vaccines that contain Hib conjugate, should never be given to a child younger than 6 weeks of age.**

All 3 conjugate Hib vaccines licensed for use in infants are interchangeable. A series that includes vaccine of more than one type will induce a protective antibody level. If it is necessary to change vaccine type, three doses of any combination constitute the primary series. Any

licensed conjugate vaccine may be used for the booster dose regardless of what was received in the primary series.

Unvaccinated children 7 months of age and older may not require a full series of 3 or 4 doses. The number of doses a child needs to complete the series depends on the child's current age.

**Detailed Vaccination Schedule
for *Haemophilus influenzae* type b Conjugate Vaccines**

Vaccine	Age at 1 st Dose (Months)	Primary Series	Booster
HbOC/PRP-T	2-6	3 doses, 2 months apart	12-15 months*
	7-11	2 doses, 2 months apart	12-15 months*
	12-14	1 dose	2 months later
	15-59	1 dose	—
PRP-OMP	2-6	2 doses, 2 months apart	12-15 months*
	7-11	2 doses, 2 months apart	12-15 months*
	12-14	1 dose	2 months later
	15-59	1 dose	—
PRP-D (Connaught)	15-59	1 dose	—

*At least 2 months after previous dose.

HbOC or PRP-T

Previously unvaccinated infants aged 2-6 months should receive three doses of vaccine administered 2 months apart, followed by a booster dose at age 12-15 months, at least 2 months after the last vaccination. Unvaccinated children aged 7-11 months should receive two doses of vaccine, 2 months apart, followed by a booster dose at age 12-15 months, at least 2 months after the last vaccination. Unvaccinated children aged 12-14 months should receive two doses of vaccine, at least 2 months apart. Any previously unvaccinated child aged 15-59 months should receive a single dose of vaccine.

PRP-OMP

Unvaccinated children aged 2-11 months should receive two doses of vaccine, 2 months apart, followed by a booster dose at 12-15 months of age, at least 2 months after the last dose. Unvaccinated children aged 12-14 months should receive two doses of vaccine, 2 months apart. Any previously unvaccinated child 15-59 months of age should receive a single dose of vaccine.

PRP-D

One dose of PRP-D may be administered to unvaccinated children aged 15-59 months. This vaccine may be used as a booster dose at 12-18 months of age following a two- or three-dose primary series, regardless of the vaccine used in the primary series. This vaccine is not licensed for use among infants because of its limited immunogenicity and variable protective efficacy in this age group.

Children with a **lapsed Hib immunization series** (that is, children who have received one or more doses of Hib-containing vaccine but are not up-to-date for their age) may not need all the remaining doses of a 3 or 4 dose series.

The ACIP does not address the issue of vaccination of children with a lapsed Hib series. However, the American Academy of Pediatrics Red Book does provide some guidance. Information from the Red Book is summarized in the following table.

**Hib Vaccination Schedule for Children with Lapsed Series
(from 2000 AAP Red Book)**

Current Age (Months)	Prior Vaccination History	Recommended Regimen
7-11	1 dose	1 dose at 7-11 mos, booster at least 2 mos later at 12-15 mos
7-11	2 doses of HbOC or PRP-T	Same as above
12-14	2 doses before 12 mos	1 dose of any licensed conjugate
12-14	1 dose before 12 mos	2 doses of any licensed conjugate separated by 2 mos
15-59	Any incomplete schedule	1 dose of any licensed conjugate

Hib invasive disease does not always result in development of protective anti-PRP antibody levels. **Children <24 months of age who develop invasive Hib disease** should be considered unimmunized and receive Hib vaccine as recommended in the schedule. Vaccination of these children should start as soon as possible during the convalescent phase of the illness. The schedule should be completed as needed for the child's age.

Vaccination of older children and adults

In general, **children >59 months of age** do not need Hib vaccination. The majority of these children are immune to Hib, probably from asymptomatic infection as infants. However, some older children and adults are at increased risk for invasive Hib disease and may be vaccinated. These high risk persons include those with functional or anatomic asplenia (e.g., sickle cell disease, postsplenectomy), immunodeficiency (in particular, persons with IgG2 subclass deficiency), immunosuppression from cancer chemotherapy, and infection with human immunodeficiency virus. Previously unvaccinated persons >59 months of age with one of these

high risk conditions should be given at least one dose of any licensed Hib conjugate vaccine.

COMBINATION VACCINES

Two combination vaccines that contain *Haemophilus influenzae* type B are available in the United States - a DTaP-Hib combination (TriHIBit[®], Aventis Pasteur), and a hepatitis B - Hib combination (COMVAX[®], Merck Vaccine Division). Combination vaccines containing whole-cell pertussis vaccine and Hib are no longer available in the United States.

TriHIBit[®]

TriHIBit was approved for use in the United States in September 1996. The vaccines are packaged together in separate vials, and the DTaP component (Tripedia[®]) is used to reconstitute the Hib component (ActHIB[®]). No other brand of DTaP and Hib vaccine may be used to produce this combination (e.g., Infanrix[®] must not be substituted for Tripedia). In addition, when supplied as TriHIBit, the DTaP and Hib components have a single lot number. Providers should generally use only the DTaP and Hib supplied together as TriHIBit. However, it is acceptable to combine Tripedia and ActHIB that have been supplied separately (i.e., not packaged as TriHIBit). In this situation, the lot numbers of both vaccines should be recorded in the child's chart.

Because of evidence of reduced immunogenicity of the Hib component when used as a combination, TriHIBit is not approved by the Food and Drug Administration for use as the primary series at 2, 4, or 6 months of age. It is approved only for the fourth dose of the DTaP and Hib series. If TriHIBit is administered as one or more doses of the primary series at 2, 4, or 6 months of age, the Hib doses should be disregarded, and the child should be revaccinated as age-appropriate for Hib. The DTaP doses may be counted as valid and do not need to be repeated.

Although TriHIBit cannot be used in the primary series at 2, 4, or 6 months of age, it may be used as the booster (final) dose following a series of single antigen Hib vaccine or combination hepatitis B - Hib vaccine (Comvax[®]). Therefore, TriHIBit can be used if the child is aged >12 months, and has received at least one prior dose of Hib vaccine >2 months earlier, and TriHIBit will be the last dose in the Hib series. For example, TriHIBit can be used for the booster dose at 12-15 months of age in a child who has received Comvax or PedvaxHib[®] at 2 and 4 months of age, or 3 prior doses of HibTiter[®] or ActHib. TriHIBit can also be used at 15-59 months of age in a child who has received at least one prior dose of any Hib-containing vaccine. TriHIBit should not be used if the child has received no prior Hib doses.

COMVAX[®]

COMVAX is a combination hepatitis B-Hib vaccine, licensed in October 1996. The vaccine contains a standard dose of PRP-OMP (PedvaxHIB[®]), and 5 micrograms of Merck's hepatitis B vaccine. COMVAX is licensed for use when both antigens are indicated. However, Hib vaccine

should not be given to infants <6 weeks of age because of the potential of immune tolerance to the Hib antigen.

COMVAX should not be used in infants <6 weeks of age (i.e., the birth dose of hepatitis B, or a dose at one month of age, if the infant is on a 0-1-6 schedule). COMVAX is not licensed for infants whose mothers are known to be hepatitis B surface antigen positive (i.e., acute or chronic infection with hepatitis B virus). However, the vaccine contains the same dose of Merck's hepatitis B vaccine recommended for these infants, so response to the hepatitis B component of COMVAX should be adequate.

ADVERSE REACTIONS FOLLOWING VACCINATION

Adverse events following Hib conjugate vaccines are uncommon. Swelling, redness, and/or pain have been reported in 5%-30% of recipients and usually resolve within 12-24 hours. Systemic reactions such as fever and irritability are infrequent. Available information on adverse events suggests that the risks for local and systemic events following TriHIBit administration are similar to those following concurrent administration of its individual component vaccines, and are probably due to the pertussis component of the DTaP vaccine.

All serious adverse events that occur after receipt of any vaccine should be reported to the Vaccine Adverse Events Reporting System (VAERS).

CONTRAINDICATIONS AND PRECAUTIONS TO VACCINATION

Vaccination with Hib conjugate vaccine is contraindicated in persons known to have experienced anaphylaxis following a prior dose of that vaccine. Vaccination should be delayed in children with moderate or severe acute illnesses. Minor illnesses (e.g., mild upper-respiratory infection) are not contraindications to vaccination. Hib conjugate vaccines are contraindicated among children <6 weeks of age because of the potential for development of immunologic tolerance.

Contraindications and precautions for the use of TriHIBit and COMVAX are the same as those for its individual component vaccines (i.e., DTaP, Hib, and hepatitis B).

VACCINE STORAGE AND HANDLING

All Hib conjugate vaccines should be shipped in insulated containers to prevent freezing. Unreconstituted or liquid vaccine should be stored at refrigerator temperature (2o-8oC [35o-46oF]). Hib vaccine must not be frozen. Hib vaccines are stable for 30 days after reconstitution if the vaccine is stored at refrigerator temperature.

Opened multidose vials may be used until the expiration date printed on the package if they are not contaminated. ActHIB and TriHIBit should be used within 24 hours of reconstitution.

SURVEILLANCE AND REPORTING OF HIB DISEASE

Invasive Hib disease is a reportable condition in most states. All health care workers should report any case of invasive Hib disease to local and state health departments.

RIFAMPIN PROPHYLAXIS

Several studies have shown that rifampin eradicated Hib carriage in >95% of contacts of primary Hib cases, including children in day-care facilities.

Contacts who develop symptoms suggestive of invasive Hib disease, such as fever or headache, should be evaluated promptly.

Rifampin chemoprophylaxis for **household contacts** is no longer indicated if all contacts aged <4 years are fully vaccinated against Hib disease. A child is considered fully immunized against Hib disease following (a) at least one dose of conjugate vaccine at 15 months of age; (b) two doses of conjugate vaccine at 12-14 months of age; or (c) two or more doses of conjugate vaccine at <12 months of age, followed by a booster dose at 12 months of age. In households with one or more infants <12 months of age (regardless of vaccination status) or with a child aged 1-3 years who is inadequately vaccinated, all household contacts should receive rifampin prophylaxis following a case of invasive Hib disease that occurs in any family member. The recommended dose is 20 mg/kg as a single daily dose (maximal daily dose 600 mg) for 4 days. Neonates (<1 month of age) should receive 10 mg/kg once daily for 4 days.

The use of rifampin in **day-care classrooms** is controversial. If a case of Hib disease has occurred, and any children less than 2 years of age have been exposed, all parents should be notified. Although data on risk are not optimal, all students (regardless of age) and staff in the classroom should receive rifampin prophylaxis according to the above regimen. However, rifampin prophylaxis is not necessary if all children <4 years of age are fully immunized.

Rifampin is contraindicated in pregnant women, as its effect on the fetus has not been established and it is teratogenic in laboratory animals.

Rifampin prophylaxis should be instituted as rapidly as possible. If more than 14 days have passed since the last contact with the index case, the benefit of rifampin prophylaxis is likely to be decreased.

The index case should be treated with the same rifampin regimen before discharge from the hospital, since antimicrobials used to treat invasive disease do not reliably eradicate carriage.

Children in day-care classrooms who are to receive chemoprophylaxis and who have received the Hib vaccine should also receive rifampin. However, if all children <4 years of age are fully immunized, chemoprophylaxis is not necessary.

Side effects may occur in up to 20% of recipients, and include nausea, vomiting, diarrhea, headache, and dizziness. Rifampin gets into body fluids exceptionally well and usually causes orange discoloration of urine. It may also cause discoloration of soft contact lenses and lens implants, or ineffectiveness of oral contraceptives.

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